et al., 1970) that atractyloside and trialkyltins act at different sites. The ATPase of broken mitochondria is inhibited by oligomycin, unlike the solubilized ATPase (Selwyn & Chappell, 1962). The soluble ATPase from acetone-dried ox heart mitochondria (Selwyn, 1967) is not inhibited by trimethyltin at concentrations up to 250 μ M. Kagawa & Racker (1966) have shown that the soluble ATPase is inhibited by tributyltin only in the presence of the factor that confers oligomycin-sensitivity on the ATPase. These observations leave little doubt that the site of action of trialkyltins is the same as that of oligomycin.

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Inhibitory Actions of Trialkyltin Compounds on Mitochondrial Respiration

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In rat liver mitochondria, trialkyltin compounds inhibit ADP-stimulated respiration at pH 7.5 and 6.8 (Aldridge, 1958; Sone & Hagihara, 1964; Stockdale *et al.*, 1970; Aldridge & Street, 1971), but inhibition of 2,4-dinitrophenol-stimulated respiration is significant only at pH 6.8 (Coleman & Palmer, 1971). Investigation of the pH-activity curves for the dinitrophenol-stimulated oxidation of succinate by mitochondria reveals that the activity is shifted to a more alkaline region by trialkyltin compounds. The pH-activity curve for mitochondria broken by freeze-thawing is not affected by dinitrophenol or by trialkyltin compounds, but closely resembles the pH-activity curve for intact mitochondria in the presence of dinitrophenol and trialkyltin compounds. The inhibition of respiration by trialkyltins on intact mitochondria at pH 6.8 in the presence of dinitrophenol is well correlated with their ability

to catalyse the Cl^- - OH^- exchange. This exchange has been shown to allow rapid pH equilibration across the mitochondrial membrane (Selwyn *et al.*, 1970), in contrast with uncoupling agents, which mediate proton uniport (Mitchell & Moyle, 1967). These observations indicate that the respiratory inhibition caused by trialkyltin compounds at pH 6.8 is a result of the equilibration of pH across the mitochondrial membrane changing the pH of the environment of respiratory enzymes to a pH where they have low activity. The absence of any inhibition on broken mitochondria is not in accord with the suggestion (Coleman & Palmer, 1971) of a direct inhibitory action on the respiratory chain, and Aldridge & Street (1971) have produced evidence that, at high substrate concentrations, depletion of intramitochondrial substrate is not an important factor in the inhibition.

In the presence of 10 mM- P_i , trialkyltins show a decreased effectiveness as inhibitors of phosphorylation as the pH is lowered from 7.5 to 6.8 (Coleman & Palmer, 1971). At pH 6.8, 10 mM- P_i greatly diminishes the effectiveness of trialkyltins as inhibitors of dinitrophenol-stimulated respiration. In a sucrose medium containing 1.0 mM- P_i , trialkyltin compounds are equally as effective as inhibitors of phosphorylation at pH 6.8 and 7.6. The pH-dependence observed by Coleman & Palmer (1971) may be due to the binding of trialkyltins to P_i , which is in agreement with the observations made by Rose (1969) and Selwyn *et al.* (1972).

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